REMARKS

Reconsideration of the rejections set forth in the Office action dated June 28, 2001 is respectfully requested. Applicant petitions the Commissioner for a 2-month extension of time; a separate petition accompanies this amendment. Claims 1-10 are currently under examination.

I. Amendments

The specification has been amended to provide a title that is clearly indicative of the invention to which the claims are directed.

The claims have been amended as set forth above. None of the claim amendments introduces a substantive limitation. No new matter has been added by these amendments.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with Markings to Show Changes Made."**

II. Rejection Under 35 U.S.C. §112, second paragraph

Claims 1-10 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 1, 4 –7 and 9 – 10 were amended according to the Examiner's suggestions.

In view of the foregoing claim amendments, Applicants submit that the claims now pending in the application meet the requirements of 35 U.S.C. §112, second paragraph.

III. Double-Patenting Rejection

Claims 1-10 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of application serial no. 09/518,178 (now U.S. Patent No. 6,300,141 B1, issued October 9, 2001). The Examiner noted that a timely filed Terminal Disclaimer in compliance with 36 C.F.R. §1.321(c) would overcome an actual or provisional rejection on this ground.

Enclosed herewith is an executed Terminal Disclaimer filed in accordance with C.F.R. §1.321(b) and (c) which disclaims the terminal portion of any patent issuing on the instant application that extends beyond the expiration of U.S. Patent No. 6,300,141 B1.

Applicants submit that Terminal Disclaimer overcomes the rejection for obviousness-type double patenting and withdrawal of the rejection is respectfully requested.

IV. Rejection Under 35 U.S.C. §103(a)

Claims 1 - 10 were rejected under 35 U.S.C. §103(a) as being obvious over Lennox *et al.* (WO 97/41424). This rejection is respectfully traversed in view of the following remarks.

A. The Invention

The present invention relies on three key features, none of which is shown or suggested in the cited prior art:

1. producing a mobile "surrogate analyte" (the solution form of the coil-forming peptide) in an amount related to the amount of analyte, for reacting with the biosensor;

2. determining the presence or amount of analyte from a biosensor signal related to the amount of surrogate that binds to the biosensor; and

3. where the interaction of the surrogate with the biosensor is unrelated to the nature of the analyte.

These features provide several advantages over the biosensor methods and devices disclosed in the cited art. In particular,

1. the ability to detect both small- and large-molecule analytes in the same assay format. In the methods described in the cited art, biosensor signal is based on the perturbation of the biosensor surface produced by the binding of an (relatively large) anti-ligand analyte to a (relatively small) ligand molecule carried on the biosensor surface. All assay formats in the prior art devices require this configuration. In the present invention, the size of the analyte is not crucial, since the biosensor is responding to the interaction between two coil-forming peptides, not a ligand/anti-ligand interaction; and

2. the ability to design multi-analyte assays with a single type of biosensor. In the prior art, each biosensor requires an analyte-specific ligand carried on its surface. In the present invention, the biosensor has the same coil-forming peptide "receptor."

B. The Cited Art

Lennox (WO 97/41424) teaches a biosensor assay device for detecting a binding event between a ligand molecule attached to a biosensor surface and an anti-ligand molecule, whose binding to the biosensor-bound ligand perturbs the biosensor surface, producing a detectable biosensor signal. An array of biosensors is also disclosed. Nowhere does Lennox show or suggest the key features of the invention noted above, or the advantages achievable thereby.

It is the Examiner's position that the reference inherently discloses obtaining a first coil forming peptide from the reaction of a sample with an analyte-reaction reagent. The Examiner's position is not understood. As described on page 6, lines 18 - 24 of the reference, two peptide subunits are constructed and assembled in a manner that anchors a ligand on the biosensor surface. The first peptide subunit is attached directly to the surface, and the second subunit is attached to the ligand. Thus, in the cited reference no solution form of a coil-forming peptide occurs from reacting a liquid sample with an analyte-reaction reagent.

The next paragraph of the reference describes the two types of analyte-binding assays contemplated in the reference. The first is where the analyte is an antiligand molecule. In this case, the analyte can bind directly to the ligand molecule carried on the biosensor, to produce a biosensor signal. The second is where the analyte is a small-molecule (ligand). In this case, the assay further requires a ligand-binding agent that can bind both to the analyte and biosensor ligand. Thus, the prior art requires two different assay formats for ligand and anti-ligand analytes, in contrast to the present invention.

Contrary to the Examiner's assertion, the reference nowhere suggests or requires reacting a liquid sample with an analyte-reaction reagent to obtain a first coil-forming peptide in solution.

C. Analysis

According to the MPEP § 2143, "to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all the claim limitations."

In the present case, the cited reference does not show or suggest the critical elements of the invention, as noted above. Even if these elements were disclosed in the cited reference, the prior art does not recognize the advantages of the invention, and thus provides no motivation for combining elements along the lines of the invention.

For the reasons presented above, claim 1 cannot be considered obvious over the cited art or any other art known to the applicants. The remaining pending claims, which depend from claim 1, define over the prior art for the same reasons that claim 1 does.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103.

V. Conclusion

In view of the above remarks, the applicants submit that the claims now pending are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4405.

Respectfully submitted,

Date: 11-28-01

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Version with Markings to Show Changes Made

In the Specification:

The title beginning on page 1, line 3, has been replaced with the following rewritten title:

Biosensor [Device and] Method for Detecting Analytes in a Liquid

In the Claims:

Claims 1, 4 – 7, and 9 – 10 have been amended as follows:

1. (Amended) A method for detecting or quantitating an analyte present in a liquid sample, comprising,

reacting the liquid sample with an analyte-reaction reagent,

by said reacting, generating a solution [form] of a first coil-forming peptide having a selected charge [and being capable of] for interacting with a second, oppositely charged coil-forming peptide to form a stable α-helical coiled-coil heterodimer,

contacting the first [coil-form] coil-forming peptide generated by said reaction with a biosensor having a detection surface with surface-bound molecules of [such] said second, oppositely charged coil-forming peptide, under conditions effective to form a stable α-helical coiled-coil heterodimer on said detection surface, where [the] binding of the [solution form of the] coil-forming peptide to the immobilized coil-forming peptide [is effective to measurably alter] measurably alters a signal generated by the biosensor, and

measuring the signal generated by the biosensor[,] to determine whether [such] said coiled-coil heterodimer formation on said detector surface has occurred.

4. (Amended) The method of claim 1, wherein said analyte is a ligand, and said reacting includes mixing the analyte with a conjugate of the first coil-forming peptide and the analyte or an analyte analog, under conditions that the conjugate is displaced from an immobilized analyte-binding anti-ligand agent [by the presence of analyte] when analyte is present.

5. (Amended) The method of claim 1, wherein the [said] analyte is an enzyme and said reacting [is effective to enzymatically release] enzymatically releases said second coil-forming

peptide in soluble form [in the presence of analyte] when analyte is present.

6. (Amended) The method of claim 1, wherein the biosensor is an electrochemical biosensor that includes a conductive detection surface, a monolayer composed of hydrocarbon chains anchored at their proximal ends to the detection surface, and the second charged coil-forming peptide also anchored to said surface, where [the] binding of the first peptide to the second peptide, to form [such] said heterodimer, [is effective to measurably alter] measurably alters current flow across the monolayer mediated by a redox ion species in an aqueous solution in contact with the monolayer, relative to electron flow observed [in the presence of] when the second peptide alone is present.

7. (Amended) The method of claim [5] 6, wherein the redox ion species has [the same charge as] a charge equal to said second coil-forming peptide, and [the] binding of the first peptide to the second peptide [is effective to enhance] enhances ion-mediated current flow across said monolayer.

9. (Amended) The method of claim [5] 6, wherein the redox ion species has a charge opposite that of said second coil-forming peptide, and [the] binding of the first peptide to the second peptide [is effective to reduce] reduces ion-mediated current flow across said monolayer.

10. (Amended) The method of claim [8] 6, wherein the redox ion species is $Fe(CN)_6^{3-}$, if the charge of said first coil-forming peptide is positive, and $Ru(NH_3)_6^{3+}$, if the charge of said first coil-forming peptide is negative.